

# A New Radiofrequency Thermal Balloon Catheter for Pulmonary Vein Isolation

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<b>OBJECTIVES</b>	We sought to evaluate whether porcine pulmonary vein (PV) isolation (PVI) can be produced by ablation using our novel radiofrequency (RF) thermal balloon catheter (RBC).
<b>BACKGROUND</b>	It has been proposed that PVI can prevent focal atrial fibrillation (AF) originating in or close to the PV.
<b>METHODS</b>	The RBC is composed of a 12F main shaft, a 4F inner tube and a balloon. Inside the balloon, there is a unipolar coil electrode with a thermocouple sensor mounted along the tube, the former to deliver RF energy (13.56 MHz) and the latter to monitor the temperature. After the presence of a PV potential was confirmed, the RBC was safely inserted into the left atrium (LA) by the trans-septal approach. Once the balloon was inflated and optimally wedged at the junction between the PV and LA, RF energy was applied for 5 min. Radiofrequency catheter ablation (RFA) was repeated up to three times, until elimination of the PV potential or dissociation between the LA and PV was observed. Finally, each heart was examined histologically.
<b>RESULTS</b>	In 18 PVs that had PV potentials, PVI was performed, resulting in success in 15 (success rate 83%, 95% confidence interval [CI] 58.0% to 96.3%; failure rate 17%, 95% CI 3.7% to 42.0%). After successful PVI, the PV potentials completely disappeared and the histologic examination revealed circumferential, transmural necrosis around the PV trunks. No major early complications, such as PV stenosis or macroscopic thrombosis, were observed.
<b>CONCLUSIONS</b>	The RBC was useful for PVI. (J Am Coll Cardiol 2001;38:2079–86) © 2001 by the American College of Cardiology

Recently, it has been shown that paroxysmal atrial fibrillation (AF) originating from one or more foci is amenable to a radical cure by radiofrequency catheter ablation (RFA) (1–5). Except for a few cases (6–11), the vast majority of these initiating foci are said to be clustered at the ostium or within the first few centimeters of the pulmonary veins (PVs) (2,5,12). This concept is supported by the fact that application of radiofrequency (RF) energy within a PV successfully terminated AF (1–5,12). However, RFA within the PVs does not completely prevent the recurrence of AF, and it occasionally induces PV stenosis, with resultant pulmonary hypertension (1,2,13–15). To avoid these complications, the creation of a transmural and circumferential lesion around the PV ostium—namely, pulmonary vein isolation (PVI) from the left atrium (LA)—is considered a good alternative (16). However, it is often difficult and time-consuming to achieve effective PVI with conventional ablation catheters, although it has been done by a few selected groups (16), even when an electroanatomic mapping system is utilized (17). For this reason, we tried to devise a novel ablation catheter in which the tip is equipped with an RF thermal balloon so that general electrophysiol-

ogists could easily and safely create a circumferential lesion around the PV ostium.

The aim of this study was to electrophysiologically and histologically evaluate whether RFA using this special radiofrequency thermal balloon catheter (RBC) could successfully induce PVI in porcine hearts.

## METHODS

All experiments were performed in accordance with the Guidelines for Animal Experimentation at Shonan Kamakura General Hospital.

**New device and animal experiment.** This original RBC (Satake Balloon, Toray Industries, Inc., Tokyo, Japan) is mechanically similar to the one we previously invented for coronary angioplasty (SST Balloon Catheter, Japan Crescent) (18,19). Its structure and usage are as follows: the instrument is composed of a 12F main, flexible lumen shaft containing a 4F inner tube and a balloon at the tip. The inner tube can be slid into the main shaft. A 0.035-in. guide wire is inserted into the central lumen of the tube, through which a contrast medium can be injected. In the space between the inner tube and the main shaft, there are Teflon-coated leads, which are connected to the thermal monitoring system and the RF current generator, and a tube with a turncock used to dilate the balloon with fluid. The tip is equipped with an oval-shaped, semi-compliant balloon with an inflated diameter of 1.5, 2.0, 2.5 or 3.0 cm, which is fixed between the distal end of the main shaft and that of

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#### Abbreviations and Acronyms

AF	= atrial fibrillation
CI	= confidence interval
CSd	= coronary sinus distal
ECG	= electrocardiogram or electrocardiographic
LAO	= left atrium or atrial ostium
PV	= pulmonary vein
PVI	= pulmonary vein isolation
RBC	= radiofrequency (thermal) balloon catheter
RF	= radiofrequency
RFA	= radiofrequency (catheter) ablation

the inner tube (Fig. 1). The balloon membrane, the shaft and the tube are made of heat-proof, antithrombotic resin. A unipolar electrode filament is coiled around the inner tube inside the balloon to deliver RF energy, along which a thermocouple sensor is mounted to monitor the intra-balloon temperature during the energy delivery. In 11 porcine hearts, we examined whether RFA using this RBC could create PVI. In these animals, the PVI procedure was performed under artificial ventilation and general anesthesia with intravenous pentobarbiturate. Heparin was administered after a successful transseptal puncture. An intravenous dose of 100 U/kg body weight, followed by repeated injections of 1,000 U, was used to keep the activated clotting time at ~300 s during the procedure.

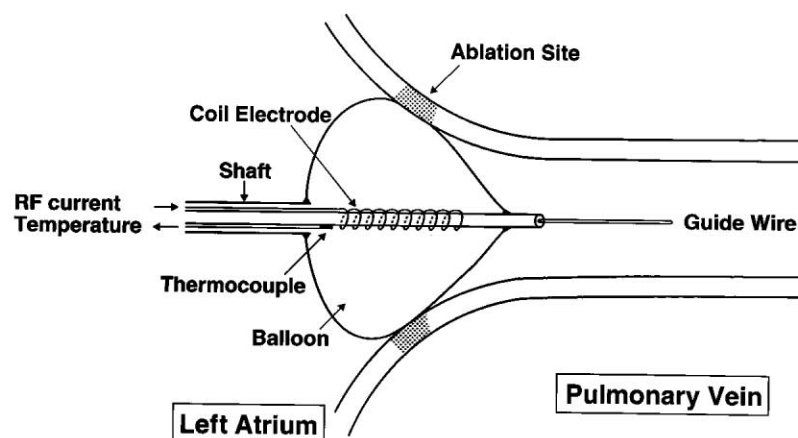
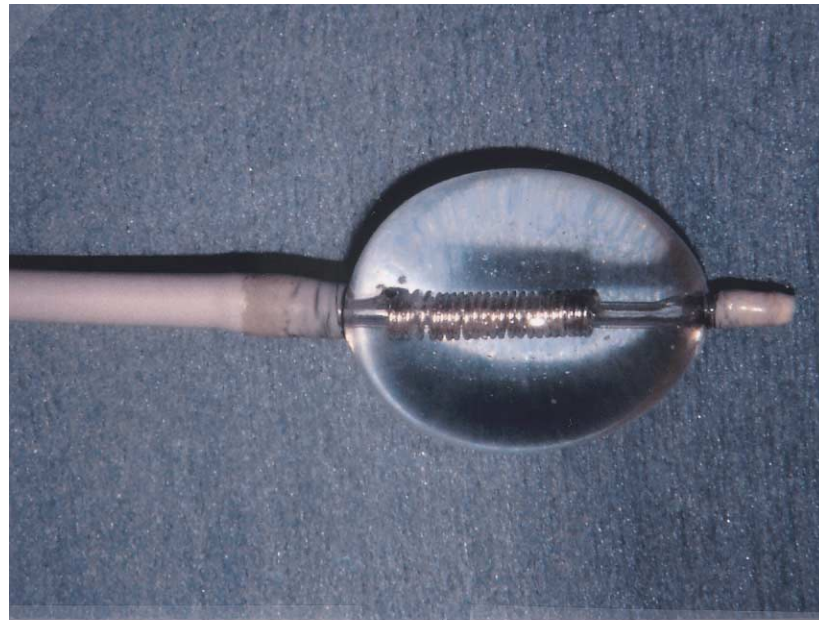
**Electrophysiologic study and RFA procedure.** The procedure was as follows: First, the right internal jugular vein and the right femoral vein were punctured, into which two 6F sheaths were inserted. In addition, a 14F sheath was introduced into the right femoral vein for the transseptal approach. A pulmonary venogram was obtained during the venous phase after injection of a contrast medium into the right atrium through a 5F angiographic catheter inserted into the femoral vein. The angiogram was continuously displayed during the procedure to precisely identify the position and size of the balloon catheter relative to the ostia of the PVs. Electrophysiologic study was then performed with two 6F quadripolar electrode catheters (5-mm inter-electrode distance and 5-mm space between each electrode pair). Bipolar intracardiac electrograms were recorded at a filter setting of 30 to 500 Hz, simultaneously with a body surface electrocardiogram (ECG). Endocardial stimulation was achieved with the stimulus intensity of twice to three times the diastolic threshold. One electrode catheter was inserted into the coronary sinus (CS) through the jugular vein under fluoroscopic guidance for pacing of and recording from the LA. A second 6F steerable electrode catheter was advanced into the LA through the transseptal sheath. This catheter was pushed into a target PV as distally as possible and then gradually pulled back until a PV potential could be recorded with the distal bipolar electrode. If no PV potential was apparent, electrical stimulation from the distal CS electrode pair was performed with a cycle length slightly shorter than that during sinus rhythm (20). After the

electrophysiologic study, the PV electrode catheter was exchanged for an RBC whose balloon diameter was 5 to 10 mm larger than that of the PV ostium. In this system, even a large balloon up to 3 cm in diameter could be inserted into the LA through the atrial septum, with a manipulation technique similar to that performed with an Inoue-balloon (Toray Industries, Inc., Tokyo, Japan)—namely, by sliding the inner tube into the main shaft with the balloon deflated. After the catheter was deployed into the LA and introduced from the PV ostium into the PV trunk upstream over a guide wire, the balloon was inflated with ~10 ml of fluid composed of physiologic saline solution and a contrast medium. Then, determination of whether or not the balloon was properly wedged at the junction between the LA and PV was done by fluoroscopically observing that the contrast medium injected into the PV through the central lumen of the inner tube did not leak into the LA (Fig. 2). Once optimal positioning of the balloon was confirmed, RF current at 13.56 MHz (Medix Generator, Nihon Medix Co., Ltd., Chiba, Japan) was delivered for 5 min between the coil electrode inside the balloon and the electric plate positioned on the body surface. The temperature inside the balloon was constantly monitored and maintained at 80°C by regulating the output of RF energy, because the difference between the temperature of the tissue contacting the balloon membrane and that at the thermal sensor during energy delivery remained at ~20°C ( $20.2 \pm 2.1^\circ\text{C}$ ) in earlier in vitro studies (data not published). This temperature difference could vary depending on the balloon diameter. To avoid such variations, the system is devised to keep the difference fixed by changing reel counts of the coil electrode according to the balloon size. After RFA was terminated and the RBC was replaced by the 6F electrode catheter, the previous stimulation and mapping protocol was repeated. The procedure was considered successful when either elimination of the PV potential or dissociation between the LA and PV potentials was confirmed. In contrast, the result was considered a failure when up to three RF applications could not induce the aforementioned conditions. The same protocol was repeated at each PV. Throughout the entire procedure, the arterial blood pressure was monitored by a pigtail catheter positioned in the ascending aorta through the femoral artery. Finally, after the entire procedure was completed, every heart was excised for gross anatomic and microscopic examinations.

**Statistical analysis.** All data are expressed as the mean value  $\pm$  SD. All data were compared by using the Student *t* test. Discrete variables (success or failure of PVI) were compared by using the Fisher exact test. A *p* value <0.05 was considered statistically significant.

## RESULTS

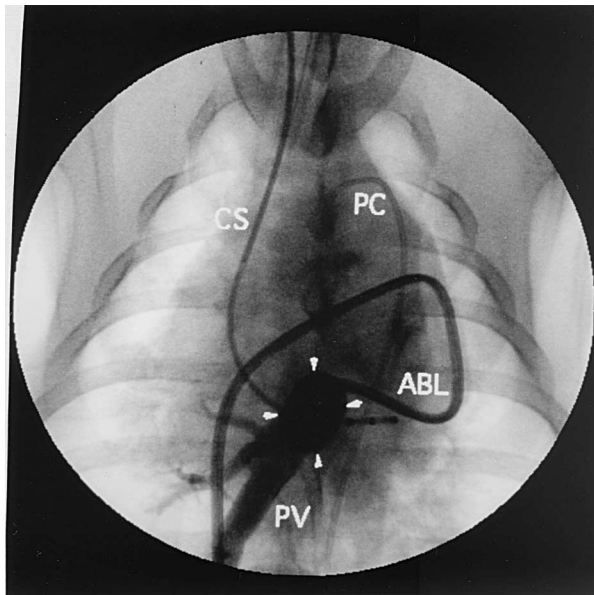
**Superior versus inferior PV.** All of the porcine hearts used in this study showed PVs anatomically dissimilar to human PVs. The most noteworthy difference was that in porcine



**Figure 1.** The radiofrequency transballoon ablation catheter used in this study. (**Top**) Photograph of a balloon 1.5 cm in diameter, inflated with fluid and equipped near the distal end of the catheter. A coil electrode with a thermocouple sensor is mounted along the tube inside the balloon. (**Bottom**) This schematic illustration shows the balloon being wedged at the junction between the pulmonary vein and left atrium. The body of the catheter is 90 cm in length, and a 12F main shaft containing a 4F inner tube, as well as its central lumen, can accept a 0.035-in. guide wire. **Shaded areas** represent the ablated sites located at the pulmonary vein ostium. See text for details. RF = radiofrequency.

hearts, there were superior and inferior PV trunks, each one branching off rightward and leftward. In all 11 pigs, the trans-septal approach was successful. However, two pigs were excluded from data analysis, because in those two hearts, it was not possible to record any spike potentials from the PVs. In the remaining nine animals, weighing between 36 and 41 kg (mean 38 kg), PVI was carried out (Table 1). Balloons with a diameter of 2.0 cm were applied to pig nos. 1 to 3, and 1.5-cm balloons were used in the remaining six pigs, according to the diameters of the PV ostia measured angiographically. Pulmonary vein isolation was successfully achieved in 15 of the 18 PVs (success rate 83%, 95% confidence interval [CI] 58.0% to 96.3%), whereas in the remaining 3 PVs (1 superior and 2 inferior

PVs), the procedure was unsuccessful (failure rate 17%, 95% CI 3.7% to 42.0%). Although the success rate was higher in superior compared with inferior PVs, the difference did not reach statistical significance (89% vs. 78%,  $p > 0.99$ ). The maximal output of the RF energy required to keep the intraballoon temperature at 80°C tended to be lower in the superior PVs ( $117 \pm 25$  W) than in the inferior PVs ( $128 \pm 44$  W). The difference was not statistically significant ( $p = 0.52$ ), however. Regarding the number of RF energy deliveries required in the superior PV, successful PVI was achieved by the first RFA in six pigs and by the second RFA in two pigs (nos. 1 and 3). In the remaining pig (no. 9), successful PVI was not accomplished by three RFA applications (Table 1). In contrast, in the inferior PV, the first



**Figure 2.** Fluoroscopically optimal image of the balloon and the inferior pulmonary vein in the anteroposterior projection. **Multiple arrows** indicate the inflated balloon filled with a mixture of saline solution and contrast medium. An occlusive pulmonary venogram confirms that the balloon is firmly wedged into the pulmonary vein ring. ABL = ablation; CS = coronary sinus electrode catheter; PC = pigtail catheter; PV = inferior pulmonary vein.

ablation was successful in six pigs and the second ablation in one pig (no. 4), whereas all attempts failed in the other two pigs (nos. 1 and 2). Thus, a slightly greater number of RF energy deliveries were needed in inferior PVs as compared with superior PVs, but the difference was insignificant ( $1.6 \pm 0.9$  and  $1.4 \pm 0.7$ , respectively;  $p = 0.77$ ). These insignificant differences may have resulted from the small number of pigs.

Arterial blood pressure dropped from a mean of 102 mm Hg to a mean of 83 mm Hg during the balloon inflation, but was restored to initial values immediately after the catheter was pulled back. During balloon inflation, the heart rate remained essentially unchanged, although a few atrial premature beats, probably originating from the PV ostium, were occasionally observed.

**Electrophysiologic isolation of PVs from the LA.** Before RFA, a dissociation between the LA and PV potentials was not observed in any PV. In 15 (8 superior and 7 inferior) of 18 PVs, elimination of the PV potential was observed after RFA, but a dissociation between the LA and PV potentials could not be demonstrated (Fig. 3). Figure 3 shows a representative successful example. The left and right panels show surface ECG and intracardiac recordings obtained before and after PVI, respectively. In each panel, the records show, from top to bottom, ECG leads I and II and intracardiac electrograms from the CS and superior PV. Before ablation, pacing from the coronary sinus-distal (CSd) was helpful to separate PV potentials (upward arrows) from a preceding low-amplitude, far-field atrial potential in the pulmonary vein-distal (PVd) electrogram (20),

revealing that the stimuli were propagated to the PV in a one-to-one fashion. In the pulmonary vein-ostium (PVo) record, however, two deflections are noted—a larger one representing the LA and a smaller one representing ventricular activation—but no PV potential is observed. After ablation, the PV potential was no longer recorded, even on the PVd electrogram during sinus rhythm (right panel) and during CSd stimulation (not shown). Moreover, the amplitude of atrial potential recorded on the PVo electrogram decreased. These findings indicate that PVI eradicated all the potentials within the superior PV (4) and brought about moderate damage to the LA myocardium around the PVo. Of course, to draw such a conclusion, one must make certain that the position of the PVo catheter remained unchanged before and after the ablation. This was verified by careful fluoroscopic observations. The average time required to finish the entire procedure was  $2.1 \pm 0.4$  h (range 1.5 to 3.0 h), including the fluoroscopy exposure of  $25 \pm 9$  min (range 14 to 37 min).

**Pathologic isolation.** In all 15 PVs in which successful PVI was achieved, circumferential, transmural necrosis around the PVo was histologically demonstrated (Fig. 4 and 5). In the remaining three PVs in which PVI was unsuccessful, noncircumferential or nontransmural necrosis, corresponding to the ablated area, was observed.

Figure 4 shows macroscopic findings in the endocardial site near the PVo after successful PVI. The ablated lesion was relatively well demarcated with brownish discoloration located at the junction between the LA and the superior and inferior PV trunks. No major early complications, such as LA or PV perforation, PV stenosis or massive clot formation, were observed after the PVI procedure. Figure 5 shows histologic specimens in Azan stain from the identical site as shown in Figure 4. The upper, middle and lower panels in Figure 5 represent low, intermediate and high magnifications, respectively. In the upper panel, transmural coagulation necrosis is noted in the LA myocardium, partly involving the atrial myocardial extension into the PV trunk. Moreover, in the middle panel, not only does contraction band necrosis surround the region of coagulation necrosis, but also endocardial and connective tissues show degenerative changes (up to 3.5 mm in depth). Edema and mild hemorrhage are frequently observed in the tissue surrounding the ablated area, as well. A minimal amount of fresh thrombus is detected on the ablated endocardium. The lower panel shows that RFA caused coagulation necrosis of myocardial fibers in the LA. There was no damage to the lung tissue, the esophagus or the aorta.

## DISCUSSION

**Major findings.** To the best of our knowledge, this is the first study in which successful PVI using an RBC was both electrophysiologically and histologically confirmed in porcine hearts. The newly designed ablation catheter was easily inserted into any target PV by the transseptal approach and

**Table 1.** Results of Radiofrequency Ablation

Pig No.	BW (kg)	Superior Pulmonary Vein			Inferior Pulmonary Vein		
		MOE (W)	No. of EDAs	PVI	MOE (W)	No. of EDAs	PVI
1	40	100	2	S	200	3	F
2	41	150	1	S	200	3	F
3	38	150	2	S	150	1	S
4	37	100	1	S	100	2	S
5	38	100	1	S	100	1	S
6	37	100	1	S	100	1	S
7	38	100	1	S	100	1	S
8	36	100	1	S	100	1	S
9	37	150	3	F	100	1	S
Mean $\pm$ SD	38.0 $\pm$ 1.6	117 $\pm$ 25	1.4 $\pm$ 0.7	89%	128 $\pm$ 44*	1.6 $\pm$ 0.9*	78%*

\*p = NS, compared with superior pulmonary vein.

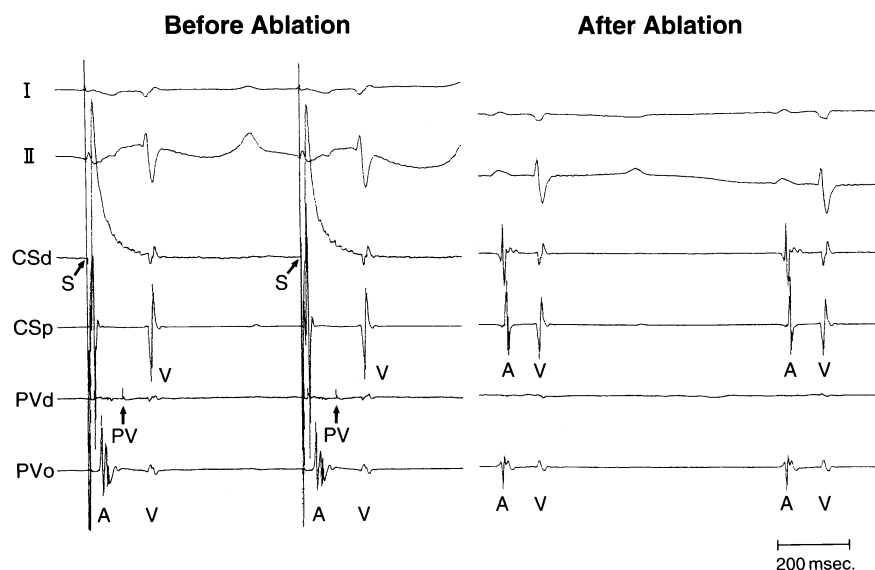
BW = body weight; EDA = energy delivery attempts; F = failure; MOE = maximal output energy required to keep the temperature inside the balloon at 80°C; PVI = pulmonary vein isolation; S = success. Under PVI, 89% and 78% indicate success rates in superior and inferior pulmonary veins, respectively.

wedged at the junction between the LA and PV trunk by dilating the semi-compliant balloon with an appropriate volume of saline and contrast medium. Whenever optimal contact between the balloon surface and the PV ring was obtained, it did not take much time, nor many attempts, to achieve successful PVI without major early complications, except for microscopic thrombus formation.

**Pulmonary vein isolation for termination of AF.** As early as 1980, an intracellular micro-electrode study in isolated guinea-pig preparations demonstrated the existence of pace-making activity in the PVs (21). Subsequent electron microscopic studies of the rat heart confirmed a close resemblance between the striated muscle of the PV and the atrial muscle, and further showed that the ultrastructural characteristics of the cells in the myocardial layer of the PV

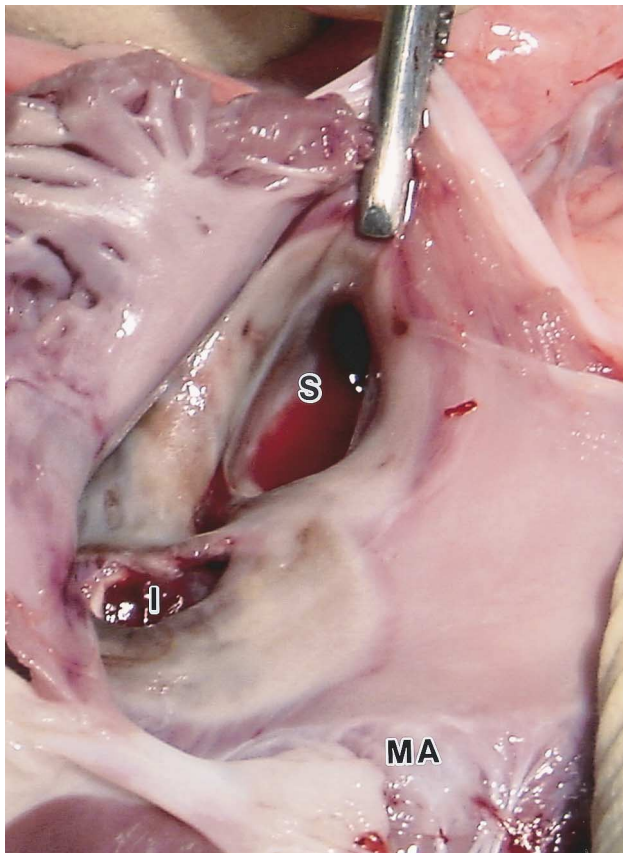
were similar to those of the sinus node cells (22). These results suggest that the myocardial cells located in the PV may well initiate atrial arrhythmias.

Recently, the myocardial sleeves within all the PVs have been shown to play an important role in the genesis of human paroxysmal or persistent AF (1-5). This contention is substantiated by the fact that AF can be terminated by ablating the PV suspected of contributing to the initiation of AF (1,2,10). However, the application of RF energy within the PV has, at least in certain instances, induced PV stenosis, leading to pulmonary hypertension (1,13,14). Furthermore, even when Haissaguerre et al. (4) performed successful PVI at the PVo by using a more segmental approach, new arrhythmogenic foci did emerge from the area proximal to the ablated lesion around the PVo (2,4,5).



**Figure 3.** Disappearance of pulmonary vein (PV) "spike" potentials after successful radiofrequency ablation. Surface electrocardiographic leads I and II are simultaneously recorded with intracardiac electrograms from the coronary sinus (CS) (CSd and CSp [d = distal and p = proximal]) and the PV (PVd and PVo [o = ostium]). (Left) Before ablation, there are PV spike potentials (PV, upward arrows) on the PVd electrogram, which are unmasked and separated from the preceding low-amplitude, far-field atrial potentials by pacing (S) from the CSd. (Right) After ablation, the PV spikes are no longer seen during sinus rhythm. Note that the amplitude of the "A" potential in the PVo electrogram decreases. A = atrial potential; V = ventricular potential. See text for details.

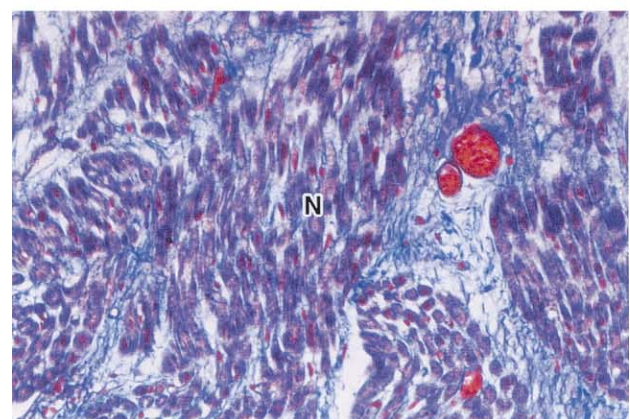
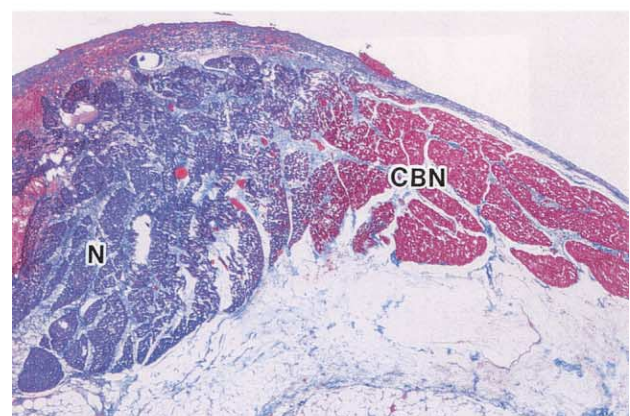
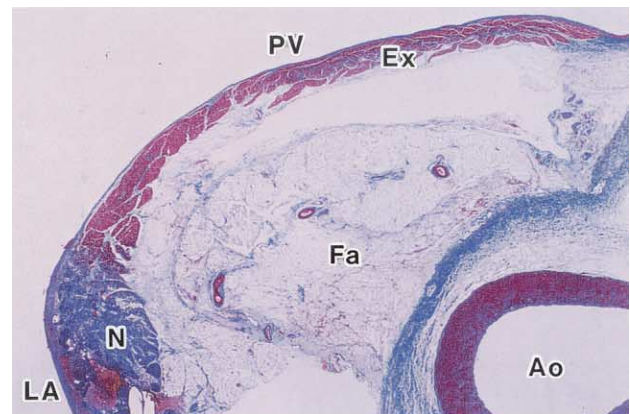




**Figure 4.** Macroscopic findings of the endocardial site after successful pulmonary vein (PV) isolation. The ablated lesion is relatively well demarcated (**brownish in color**) and located near the junction between the left atrium and PV trunks. Note that the ostia of the superior (S) and inferior (I) PVs are encircled by the ablated lesion. MA = mitral annulus. See text for details.

To prevent the recurrence of AF, circumferential ablation around the PVo, as proposed by Pappone *et al.* (16,17), is considered more useful than the previous methods (1,2,4). When using conventional ablation catheters, however, it is often time-consuming and difficult to create a circular lesion around the PVo, although it has been done by a few groups (16). Thus, it was considered desirable to develop a special ablation device for PVI. Natale *et al.* (23) showed that PVI using a new ultrasound balloon ablation system was effective in preventing recurrent human AF without early or late complications, including PV stenosis. Although our system may appear similar to theirs, there are two definite differences—one is the energy source and the other is the ablation site. Namely, they targeted the PV wall using ultrasound, whereas we mainly ablated the LA tissue around the PVo with RF energy.

**Mechanism and advantages of the thermal balloon ablation system.** **MECHANISM.** Radiofrequency application at a very high frequency (13.56 MHz), using this system, provokes a unique capacitive-type heating all around the coil electrode inside the balloon, so that the LA tissue in contact with this balloon is effectively heated (24). In contrast, the endothelium of the PV distal to the balloon is exposed to



**Figure 5.** Histologic findings of the identical case as in Figure 4. (**Top**) (low magnification): Transmurular coagulation necrosis (N) is detected near the junction (**curved portion**) between the (LA) and the inferior pulmonary vein (PV) trunk. Atrial myocardial extension (Ex) (about 9 mm in length) spreads into the PV almost entirely and reaches near the right end of the panel. Fa = fat tissue; Ao = aorta. (**Middle**) (intermediate magnification): Coagulation necrosis (N) in the LA myocardium and contraction band necrosis (CBN) in the proximal portion of the atrial myocardial extension into the PV. (**Bottom**) (high magnification): Coagulation necrosis (N) of muscle fibers located within the ablated LA. All specimens are in Azan stain.

much less heat than is the LA, because the blood surrounding the balloon has an impedance too low to be affected by the capacitive-type heating and is constantly circulating along with convection. Therefore, the tissue contacting the

balloon surface was selectively ablated (Fig. 1, shaded areas in lower panel).

**ADVANTAGES.** The major advantages of our catheter are as follows: first, once an optimal position of the balloon, with reference to the PVo, is confirmed by observation of an occlusive pulmonary venogram, application of RF energy can effectively produce a transmural circular lesion around the PVo, resulting in successful ablation of the posterior LA around the PV ostia and elimination of PV potentials, without an additional delivery of energy. Moreover, it is possible that reconditioning of the electrical activity in this relatively large zone of the LA may eventually succeed in curing AF. Second, because the interface in direct contact with the endocardium is not the electrode tip, but rather the balloon surface, the risk of causing mechanical injury to the endocardium or perforation is minimized. Finally, the use of RF energy and antithrombotic material in the balloon membrane prevents activation of the coagulation factor and massive clot formation. This merit has already been proven in coronary angioplasty using our previous RF “hot” balloons (18,19).

**Study limitations.** Admittedly, this study has several limitations. First, precise information is not available on the temperature of the interface between the PV and the balloon during RF application. However, it is known that the difference between the temperature of the interface in contact with the balloon surface and that inside the balloon during RF application is  $\sim 20^{\circ}\text{C}$ , as determined in earlier in vitro studies (data not published). Second, if a direct connection between the atrial tissue and the distal portion of the PV were indeed present in some human hearts (25), even successful PVI procedures might not eradicate focal AF. Third, it has not been evaluated whether the PVI procedure could cause a persistent disturbance of mechanical atrial function (26), including a left-to-right shunt, or adversely affect the secretion of atrial natriuretic peptide hormone (27), as in the case of multiple linear RF lesions, although a hemodynamic disturbance was not observed during the early phase of the present study. Finally, it is unknown whether complete isolation of the LA and PVs could somehow create a new arrhythmogenic substrate for macro-reentrant atrial tachyarrhythmias, such as LA flutter (28). To solve this problem, further studies must be conducted on the need of an additional ablation line connecting the PV and the mitral annulus (17,29,30).

**Clinical implications.** In this experiment, 5 min was adopted as the RF delivery time. This is because we wanted to clearly demonstrate the effect of capacitive-type heating on the tissue. However, the pathologic examination showed excessive damage to the LA myocardium. Hence, in the clinical setting, we would limit the duration of RF energy application to 2 to 3 min. We are now improving the RBC system by reducing the diameter of the shaft and the temperature difference between the thermocouple sensor and the contacting tissue by changing the shape of the balloon.

**Conclusions.** We have demonstrated, both electrophysiologically and histologically, that RFA using our novel thermal balloon system is feasible for the creation of circumferential lesions around porcine PV rings, without major early complications. We expect that this system would be a new tool for the treatment of patients with paroxysmal AF originating in the PV or around the PV ostium, or both.

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